

AMENDMENTS TO THE CLAIMS

1. (Original) A method for diagnosing a susceptibility to cardiovascular disease especially myocardial infarction (MI) and stroke in a subject by detecting genetic variation or polymorphism, i.e. a mutation, in at least three of the genes selected from the group consisting of:

- (a) α_{2B} -adrenoceptor
- (b) apolipoprotein B
- (c) dimethylarginine dimethylaminohydrolase 1
- (d) fibrinogen-beta
- (e) neuropeptide Y
- (f) natriuretic peptide precursor A
- (g) cystathione beta synthase
- (h) glycoprotein IIb/IIIa
- (i) lipoprotein lipase

comprising the steps of:

- i) providing a biological sample of the subject to be tested,
- ii) detecting the presence of mutations in the genes, the presence of a mutation in one or several of the genes indicating an increased risk of coronary heart disease (CHD) and/or myocardial infarction (MI) in said subject.

2. (Original) The method according to claim 1, wherein the detection step is a nucleic acid assay.

3. (Original) The method according to claim 2, wherein the detection step is carried out using a gene or DNA chip, microarray, strip, panel or similar combination of more than one genes, mutations or RNA expressions to be assayed.

4. (Original) The method according to claim 2, wherein the polymorphisms are determined using polymerase chain reaction.

5. (Original) The method according to claim 1, wherein the biological sample is a blood sample or buccal swab sample.

6. (Original) The method according to claim 1, further comprising a step of combining information concerning age, gender, the family history of cardiovascular diseases and hypercholesterolemia, and the medical history concerning cardiovascular diseases of the subject with the results obtained from step ii) of the method for confirming the indication obtained from the detection step.

7. (Original) The method according to claim 1, wherein said information is about hypercholesterolemia in the family, smoking status, CHD in the family, history of cardiovascular disease, obesity in the family, and waist-to-hip circumference ratio (cm/cm)

8. (Original) The method according to claim 1, wherein said information is about antihypertensive medication, smoking status, frequency of hangovers and body mass index.

9. (Original) The method according to claim 1, further comprising a step determining blood, serum or plasma cholesterol, HDL cholesterol, LDL cholesterol, triglyceride, apolipoprotein B and AI, fibrinogen, ferritin, transferring receptor, C-reactive protein, serum concentration or plasma insulin concentration.

10. (Original) The method according to claim 1, wherein the selected genes are natriuretic peptide precursor A, α_{2B} -adrenoceptor, apolipoprotein B and dimethylarginine dimethylaminohydrolase 1.

11. (Original) The method according to claim 1, wherein the selected genes are fibrinogen-beta, α_{2B} -adrenoceptor and neuropeptide Y.

12. (Original) The method according to claim 1 further comprising a step of determining height, weight, systolic and diastolic blood pressure, heart rate, maximal oxygen uptake, or other electrocardiographic measurement of the subject.

13. (Original) The method according to claim 10, wherein the detected mutations are Val32Met of natriuretic peptide precursor A, an insertion/deletion of three glutamic acids in the region of 12 Glu aminoacids in the codons 298-309 of α_{2B} -adrenoceptor, Thr98Ile of apolipoprotein B and SNP IVS2-33C>T of dimethylarginine dimethylaminohydrolase 1.

14. (Original) The method according to claim 11, wherein the detected mutations are SNP – 455G>A of fibrinogen-beta, an insertion or deletion of three glutamic acids in the region of 12 Glu aminoacids in the codons 298-309 of α_{2B} -adrenoceptor, and SNP –52C>G of neuropeptide Y.

15. (Currently Amended) The method according to ~~any one of the preceding claims~~ claim 1 further comprising a step of calculating the probability of a cardiovascular disease using a logistic regression equation as follows:

Probability of a cardiovascular disease = $[1 + e^{(-a + \sum(b_i \cdot X_i))}]^{-1}$, where e is Napier's constant, X_i are variables related to the cardiovascular disease, b_i are coefficients of these variables in the logistic function, and a is the constant term in the logistic function.

16. (Original) The method according to claim 15, wherein a and b_i are determined in the population in which the method is to be used.

17. (Original) The method according to claim 15, wherein X_i are selected among the variables that have been measured in the population in which the method is to be used.

18. (Original) The method according to claim 15, wherein b_i are between the values of -20 and 20.

19. (Original) The method according to claim 15, wherein X_i are binary variables that can have values or are coded as 0 (zero) or 1 (one).

20. (Original) The method according to claim 15, wherein i are between the values 0 (none) and 100,000.

21. (Original) A kit for diagnosing a susceptibility to a cardiovascular disease especially myocardial infarction (MI) and stroke in a subject, comprising means for detecting genetic variation or polymorphism, i.e. a mutation, in at least three of the genes selected from the group consisting of:

- (a) α_{2B} -adrenoceptor
- (b) apolipoprotein B
- (c) dimethylarginine dimethylaminohydrolase 1

- (d) fibrinogen-beta
- (e) neuropeptide Y
- (f) natriuretic peptide precursor A
- (g) cystathione beta synthase
- (h) glycoprotein IIb/IIIa
- (i) lipoprotein lipase

and optionally software to interpret the results of the detection.

22. (Original) The kit according to claim 21, comprising a DNA chip, microarray, DNA strip, DNA panel or real-time PCR based tests.

23. (Original) The kit according to claim 21, comprising a questionnaire for obtaining patient information concerning age, gender, height, weight, the family history of cardiovascular diseases and hypercholesterolemia, the medical history concerning cardiovascular diseases.